CLAIMS:

1. A native complement pathway protein modified such that the protein is capable of forming a down-regulation resistant C3 convertase.

2. A protein as claimed in claim 1 which is a modified human protein.

3. A protein as claimed in claim 1 or claim 2 which is more resistant to cleavage by factor I than the native protein.

4. A protein as claimed in any one of claims 1 to 3 which is a modified C3 protein.

5. A protein as claimed in claim 4 wherein the protein is modified by replacement of either Arg-1303, Arg-1320,or both by another amino acid.

6. A protein as claimed in claim 5 wherein Arg-1303, Arg-1320 or both are replaced by glutamine, tyrosine, cystine, tryptophan, glutamic acid or glycine.

7. A protein as claimed in claim 6, wherein Arg-1320 is replaced by glutamine.

8. A protein as claimed in claim 6 or 7, wherein Arg-1303 is replaced by glutamic acid, glycine or glutamine.

9. A protein according to any preceding claim which has reduced susceptibility to Factor H and/or Factor I relative to native human C3, said protein having one or more amino acid changes relative to native human C3 in

the region corresponding to amino residues 752-754 and/or residues 758-780 of native human C3.

10. A protein according to claim 9 wherein the one or more amino acid changes are changes from acidic amino acid residues to neutral amino acid residues.

11. A protein according to claim 9 or claim 10 wherein the amino acid residue changes are changes from Asp-Glu-Asp to Gly-Ser-Gly.

12. A protein according to any preceding claim having amino acid changes relative to native human C3 at amino acid residues corresponding to residues 1427, 1431 and/or 1433 of native human C3.

13. A protein according to any preceding claim which includes one or more mutations relative to amino acid residues 992-1005 (EDAVDAERLKHLIV) of human C3, such that the C3b and C3i products, or their derived C3 convertases, are resistant to the complement inhibitory activity of Factor H.

14. A protein according to claim 13 which includes one or more mutations relative to amino acid residues 992 (E), 993 (D), 996 (D), 997 (A), 998 (E), 999 (R), 1000 (L), 1001 (K), 1002 (H), 1005 (V) of human C3.

15. A protein according to claim 14 which includes one or more of the following mutations E992S, D993A, D996S, A997Q, E998S, R999G, L1000M, K1001N, H1002I and V1005H.

16. A protein according to any preceding claim which includes one or more mutations relative to amino acid

residues 1152-1155 (QEAK) of human C3, such that the C3b and C3i products, or their derived C3 convertases, are resistant to the complement inhibitory activity of Factor H.

17. A protein according to claim 16 which includes one or more mutations relative to amino acid residues 1152 (Q), 1153 (E) and 1155 (K) of C3.

18. A protein according to claim 17 which includes one or more of the following mutations Q1152R, E1153K and K1155F.

19. A protein according to any of claims 13 to 18 which is resistant to the complement inhibitory activity of CR1, MCP and/or DAF.

20. A protein according to any preceding claim which has one or more amino acid deletions, substitutions or insertions relative to amino acids 1546-1663 of native human C3; wherein said protein has reduced susceptibility to Factor H and/or Factor I, relative to native human C3.

21. A protein according to claim 20 comprising one or more amino acid deletions relative to amino acids 1546-1663 of native human C3.

22. A protein according to claim 20 or 21 comprising a deletion of all amino acids corresponding to amino acids 1546-1663 of native human C3.

23. A protein according to claim 20 comprising one or more different amino acids relative to native human C3 at a region corresponding to amino acid residues 1546-1663

of native human C3.

24. A protein according to claim 23 wherein the amino acids at the region corresponding to amino acids 1546-1663 of native human C3 can result from a frame-shift mutation in DNA encoding said native human C3.

25. A protein according to any of claims 20 to 24 which has one or more amino acid deletions, substitutions or insertions relative to amino acids 1636-1663 of native human C3; wherein said protein has reduced susceptibility to Factor H and/or Factor I, relative to human C3.

26. A protein according to claim 25 comprising one or more amino acid deletions relative to amino acids 1636-1663 of native human C3.

27. A protein according to claim 25 or 26 comprising a deletion of all amino acids corresponding to amino acids 1636-1663 of native C3.

28. A protein according to claim 25 comprising one or more different amino acids relative to native human C3 at a region corresponding to amino acid residues 1636-1663 of native human C3.

29. A protein acccording to claim 25 comprising one or more amino acid deletions substitutions or insertions relative to amino acids 1649-1660 of native human C3; wherein said protein has reduced susceptibility to Factor H and/or Factor I, relative to human C3.

30. A protein according to any preceding claim which has one or more amino acid deletions substitutions or insertions relative to amino acid residues 954 and/or 955

of native human C3 and which has a reduced susceptibility to cofactor-dependent (e.g. CR1 or Factor H) Factor I-mediated cleavage at this position.

31. A protein according to claim 30 in which the amino acid residue at the position corresponding to residue 954 of human C3 is different from residue 954 of human C3, which protein has reduced susceptibility to cofactor dependent (e.g. CR1 or Factor H) Factor I-mediated cleavage at said position.

32. A protein according to claim 31 in which said amino acid residue is glutamic acid, and which has reduced susceptibility to cofactor dependent (e.g. CR1 or Factor H) Factor I-mediated cleavage at said position.

33. A protein according to claim 30 in which the amino acid residues at positions corresponding to residue 954 and residue 955 of human C3 are glutamine and glycine respectively which protein has reduced susceptibility to cofactor dependent (e.g. CR1 or Factor H) Factor I-mediated cleavage at said position.

34. A protein according to claim 30 in which the amino acid residue at a position corresponding to residue 955 of human C3 is different from residue 955 of human C3, which protein has reduced susceptibility to cofactor dependent (e.g. CR1 or Factor H) Factor I-mediated cleavage at said position.

35. A fragment or a variant of a protein according to any preceding claim, said fragment or variant having C3 convertase activity and also having resistance to the complement inhibitory activity of Factor H, Factor I, CR1, MCP and/or DAF.

36. A DNA sequence coding for a protein as claimed in any one of claims 1 to 34 or for a fragment or a variant as claimed in claim 35.

37. A DNA construct (e.g. a vector) comprising a DNA sequence as defined in claim 36.

38. A protein as defined in any one of claims 1 to 34 or a fragment or variant as claimed in claim 35 for use in therapy.

39. A conjugate comprising a protein as defined in any one of claims 1 to 34 or a fragment or variant as claimed in claim 35 linked to a specific binding moiety.

40. A conjugate as claimed in claim 39 wherein the specific binding moiety is a specific binding protein.

41. A conjugate as claimed in claim 40 wherein the specific binding protein is an antibody or antigen binding fragment thereof.

42. The use of a protein as defined in any one of claims 1 to 34, or a fragment or variant as defined in claim 35, or a conjugate as defined in any one of claims 39 to 41 in the manufacture of a medicament for use in depleting levels of complement pathway protein.

43. The use as claimed in claim 42 wherein the medicament is for use in preventing rejection of foreign matter.

44. The use as claimed in claim 42 wherein the medicament is for use in localising and/or amplifying endogenous complement protein conversion and deposition

at a specific site.

45. A pharmaceutical formulation comprising one or more proteins as defined in any one of claims 1 to 34, or a fragment or variant as defined in claim 35, or a conjugate as defined in any one of claims 39 to 41 together with one or more pharmaceutically acceptable carriers or excipients.

46. A pharmaceutical formulation as claimed in claim 45 which is for use in depleting levels of complement pathway protein.

47. A pharmaceutical formulation as claimed in claim 45 which is for use in preventing rejection of foreign matter.

48. A pharmaceutical formulation as claimed in claim 45 which is for use in localising and/or amplifying complement protein conversion and deposition at a specific site.

49. A method of reducing complement pathway protein in a mammal which comprises administering to the mammal a protein as defined in any one of claims 1 to 34, or a fragment or variant as defined in claim 35, or a conjugate as defined in any of claims 39 to 41.

50. A method as claimed in claim 49 wherein administration occurs using a pharmaceutical formulation as defined in claim 45.